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=> s NIS
L1 7060 NIS

=> s breast or mammary or mamma
L2 867613 BREAST OR MAMMARY OR MAMMA

=> s l1 and l2
L3 204 L1 AND L2

=> s l3 and py<2001
 2 FILES SEARCHED...
 6 FILES SEARCHED...
L4 78 L3 AND PY<2001

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PROCESSING COMPLETED FOR L4
L5 27 DUP REM L4 (51 DUPLICATES REMOVED)

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L5 ANSWER 1 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:900398 CAPLUS
DOCUMENT NUMBER: 134:37012
TITLE: Adenovirus vectors carrying the **NIS** gene for
 sodium/iodide symporter and their use in the
 radiotherapy of cancer with iodine-131
INVENTOR(S): Perricaudet, Michel; Schlumberger, Martin; Yeh,
 Patrice; Boland-auge, Anne
PATENT ASSIGNEE(S): Aventis Pharma S.A., Fr.
SOURCE: PCT Int. Appl., 38 pp.
 CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2000076450 A2 20001221 WO 2000-FR1594 20000608 <--
WO 2000076450 A3 20010628

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
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CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2794771 A1 20001215 FR 1999-7449 19990611 <--

AU 2000055407 A5 20010102 AU 2000-55407 20000608

EP 1187919 A2 20020320 EP 2000-940476 20000608

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

JP 2003501107 T2 20030114 JP 2001-502790 20000608

PRIORITY APPLN. INFO.:

FR 1999-7449 A 19990611

WO 2000-FR1594 W 20000608

AB The invention concerns the field of gene therapy and the treatment of tumors. More particularly, the invention concerns the insertion of a gene coding for the iodine specific carrier (Na⁺/I⁻ symporter) (**NIS**) in tumor cells using an adenoviral vector to promote the accumulation of iodine in said cells. The invention also concerns the defective recombinant adenoviruses for replication comprising the **nis** gene and the use of said vectors in a method for treating cancers combining **nis** gene transfer into tumor cells and metabolic radiotherapy. Use of an adenovirus carrying the **nis** gene under control of the cytomegalovirus immediate-early promoter to confer iodide uptake on animal cells is demonstrated. Higher levels of perchlorate sensitive iodide uptake were found in transgenic SiHa cells than in the pos. control line FRTL-5. Nude mice inoculated with MRC5 cells were subsequently infected with the virus. Scintigraphy showed iodide accumulation in the thyroid and stomach (where the transporter is active), the bladder, and in the implanted tumor.

L5 ANSWER 2 OF 27 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2000406940 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10890895

TITLE: Retinoic acid induces sodium/iodide symporter gene expression and radioiodide uptake in the MCF-7 **breast** cancer cell line.

AUTHOR: Kogai T; Schultz J J; Johnson L S; Huang M; Brent G A

CORPORATE SOURCE: Molecular Endocrinology Laboratory, West Los Angeles Veterans Affairs Medical Center, Departments of Medicine and Physiology, University of California School of Medicine, Los Angeles, CA 90073, USA.

SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2000 Jul 18) 97 (15) 8519-24.

Journal code: 7505876. ISSN: 0027-8424.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200008

ENTRY DATE: Entered STN: 20000901

Last Updated on STN: 20030204

Entered Medline: 20000824

AB The sodium/iodide symporter (**NIS**) stimulates iodide uptake in normal lactating **breast**, but is not known to be active in nonlactating **breast** or **breast** cancer. We studied **NIS** gene regulation and iodide uptake in MCF-7 cells, an estrogen

receptor (ER)-positive human **breast** cancer cell line. All-trans retinoic acid (tRA) treatment stimulated iodide uptake in a time- and dose-dependent fashion up to approximately 9.4-fold above baseline. Stimulation with selective retinoid compounds indicated that the induction of iodide uptake was mediated by retinoic acid receptor. Treatment with tRA markedly stimulated **NIS** mRNA and immunoreactive protein (approximately 68 kDa). tRA stimulated **NIS** gene transcription approximately 4-fold, as shown by nuclear run-on assay. No induction of iodide uptake was observed with RA treatment of an ER-negative human **breast** cancer cell line, MDA-MB 231, or a normal human **breast** cell line, MCF-12A. The iodide efflux rate of tRA-treated MCF-7 cells was slow ($t(1/2) = 24$ min), compared with that in FRTL-5 thyroid cells ($t(1/2) = 3.9$ min), favoring iodide retention in MCF-7 cells. An in vitro clonogenic assay demonstrated selective cytotoxicity with $(^{131})\text{I}$ after tRA stimulation of MCF-7 cells. tRA up-regulates **NIS** gene expression and iodide uptake in an ER-positive **breast** cancer cell line. Stimulation of radioiodide uptake after systemic retinoid treatment may be useful for diagnosis and treatment of some differentiated **breast** cancers.

L5 ANSWER 3 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
 ACCESSION NUMBER: 2000:702982 SCISEARCH
 THE GENUINE ARTICLE: 352NK
 TITLE: Msh2, Mlh1, Fhit, p53, Bcl-2, and Bax expression in
 invasive and in situ squamous cell carcinoma of the
 uterine cervix
 AUTHOR: Giarnieri E; Mancini R; Pisani T; Alderisio M; Vecchione A
 (Reprint)
 CORPORATE SOURCE: UNIV ROMA LA SAPIENZA, FAC MED 2, SCH MED, DEPT EXPT MED &
 PATHOL, PIAZZA SASSARI 3, I-00161 ROME, ITALY (Reprint);
 UNIV ROMA LA SAPIENZA, FAC MED 2, SCH MED, DEPT EXPT MED &
 PATHOL, I-00161 ROME, ITALY
 COUNTRY OF AUTHOR: ITALY
 SOURCE: CLINICAL CANCER RESEARCH, (SEP 2000) Vol. 6, No.
 9, pp. 3600-3606.
 Publisher: AMER ASSOC CANCER RESEARCH, PO BOX 11806,
 BIRMINGHAM, AL 35202.
 ISSN: 1078-0432.
 DOCUMENT TYPE: Article; Journal
 FILE SEGMENT: CLIN
 LANGUAGE: English
 REFERENCE COUNT: 59

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB To analyze relevant factors and their effects on neoplastic progression in cervical carcinoma, a panel of genetic markers was studied. Paraffin-embedded tissue sections were obtained from 37 patients with carcinoma of the uterine cervix, 14 noninvasive squamous cell carcinomas (**NIS**-CCs), and 23 invasive squamous cell carcinomas (ISCCs). Immunoreactivity of Msh2, Mlh1, Fhit, p53, Bcl-2, and Pax proteins was examined by immunohistochemical staining with appropriate antibodies. Positive staining of Msh2 was detected in 13 of 14 (92.9%) NISCCs and in 13 of 23 (56.5%) ISCCs ($P < 0.02$), Mlh1 immunoreactivity was observed in 10 of 14 (71.4%) NISCCs and in 8 of 23 (34.8%) ISCCs ($P < 0.04$), Overexpression of p53 protein was found in 4 of 14 (28.6%) NISCCs and in 16 of 23 (69.6%) ISCCs ($P < 0.02$), Bcl-2 overexpression was detected in 2 of 14 (14.3%) NISCCs and in 15 of 23 (65.2%) ISCCs ($P < 0.003$). No significant difference in the two types of lesion was found for Pax and Fhit expression. The relationship between Mlh1, Msh2, and p53 protein expression was significant ($P < 0.001$ and $P < 0.001$, respectively), as was that between Fhit and Pax immunoreactivity ($P < 0.02$). In conclusion, we consider that altered expression of Msh2, Mlh1, p53, and Bcl-2 may be a critical event during cervical cancer progression, whereas Fhit may be a component of a proapoptotic pathway.

L5 ANSWER 4 OF 27 MEDLINE on STN DUPLICATE 2
 ACCESSION NUMBER: 2000393110 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10910060
 TITLE: Adenovirus-mediated transfer of the thyroid sodium/iodide symporter gene into tumors for a targeted radiotherapy.
 AUTHOR: Boland A; Ricard M; Opolon P; Bidart J M; Yeh P; Filetti S; Schlumberger M; Perricaudet M
 CORPORATE SOURCE: UMR1582 CNRS-IGR-Rhone-Poulenc, Villejuif, France.. boland@igr.fr
 SOURCE: Cancer research, (2000 Jul 1) 60 (13) 3484-92.
 Journal code: 2984705R. ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200008
 ENTRY DATE: Entered STN: 20000824
 Last Updated on STN: 20000824
 Entered Medline: 20000817

AB The Na⁺/I⁻ symporter (**NIS**) present in the membranes of thyroid cells is responsible for the capacity of the thyroid to concentrate iodide. This allows treatment of thyroid cancers with ¹³¹I. We propose to enlarge this therapeutic strategy to nonthyroid tumors by using an adenoviral vector to deliver the **NIS** gene into the tumor cells. We constructed a recombinant adenovirus encoding the rat **NIS** gene under the control of the cytomegalovirus promoter (Ad**NIS**). Infection of SiHa cells (human cervix tumor cells) with Ad**NIS** resulted in perchlorate-sensitive ¹²⁵I uptake by these cells to a level 125-225 times higher than that in noninfected cells. Similar results were obtained for other human tumor cell lines, including MCF7 and T-47D (**mammary** gland), DU 145 and PC-3 (prostate), A549 (lung), and HT-29 (colon), demonstrating that the Ad**NIS** vector can function in tumor cells of various origins. In addition, Ad**NIS**-infected tumor cells were selectively killed by exposure to ¹³¹I, as revealed by clonogenic assays. To assess the efficiency of this cancer gene therapy strategy in vivo, we injected the Ad**NIS** vector in human tumors (SiHa or MCF7 cells) established s.c. in nude mice. Immunohistological analysis confirmed the expression of the **NIS** protein in the tumor. Three days after intratumoral injection, Ad**NIS**-treated tumors could specifically accumulate ¹²⁵I or ¹²³I, as revealed by kinetics and imaging experiments. A quantitative analysis demonstrated that the uptake in Ad**NIS**-injected tumors was 4-25 times higher than that in nontreated tumors. On average, 11% of the total amount of injected ¹²⁵I could be recovered per gram of Ad**NIS**-treated tumor tissue. Altogether, these data indicate that Ad**NIS** is very efficient in triggering significant iodide uptake by a tumor, outlining the potential of this novel cancer gene therapy approach for a targeted radiotherapy.

L5 ANSWER 5 OF 27 MEDLINE on STN DUPLICATE 3
 ACCESSION NUMBER: 2000413175 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10946907
 TITLE: Hormonal regulation of radioiodide uptake activity and Na⁺/I⁻ symporter expression in **mammary** glands.
 AUTHOR: Cho J Y; Leveille R; Kao R; Rousset B; Parlow A F; Burak W E Jr; Mazzaferri E L; Jhiang S M
 CORPORATE SOURCE: Department of Physiology and Cell Biology, Ohio State University, Columbus 43210-1218, USA.
 SOURCE: Journal of clinical endocrinology and metabolism, (2000 Aug) 85 (8) 2936-43.
 Journal code: 0375362. ISSN: 0021-972X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English

FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000907
Last Updated on STN: 20000907
Entered Medline: 20000831

AB The observation that radioiodide uptake (RAIU) activity, mediated by the Na⁺/I⁻ symporter (**NIS**), is significantly increased in lactating **breast** suggests that RAIU and **NIS** expression in **mammary** gland are modulated by hormones involved in active lactation. We showed that both the **NIS** expression level and RAIU in rat **mammary** gland are maximal during active lactation compared to those in the **mammary** glands of virgin and pregnant rats as well as the involuting **mammary** gland. In the lactating **mammary** gland, **NIS** is clustered on the basolateral membrane of alveolar cells as a lesser glycosylated form than **NIS** in thyroid. The RAIU of lactating **mammary** gland was partially inhibited by treatment with a selective oxytocin antagonist or bromocriptine, an inhibitor of PRL release. These findings suggest that RAIU and **NIS** expression in **mammary** gland are at least in part modulated by oxytocin and PRL. Indeed, we showed that **NIS** messenger ribonucleic acid level was increased in a dose-dependent manner by oxytocin and PRL in histocultured human **breast** tumors.

L5 ANSWER 6 OF 27 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2001041773 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11079502
TITLE: Establishment and characterization of a **breast** cancer cell line expressing Na⁺/I⁻ symporters for radioiodide concentrator gene therapy.
COMMENT: Comment in: J Nucl Med. 2001 Jun;42(6):987-8. PubMed ID: 11390567
AUTHOR: Nakamoto Y; Saga T; Misaki T; Kobayashi H; Sato N; Ishimori T; Kosugi S; Sakahara H; Konishi J
CORPORATE SOURCE: Department of Nuclear Medicine and Diagnostic Imaging, Graduate School of Medicine, Kyoto University, Japan.
SOURCE: Journal of nuclear medicine : official publication, Society of Nuclear Medicine, (2000 Nov) 41 (11) 1898-904. Journal code: 0217410. ISSN: 0161-5505.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200012
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20020911
Entered Medline: 20001207

AB ¹³¹I therapy is a widely accepted treatment for metastatic differentiated thyroid cancer. To investigate the feasibility of ¹³¹I therapy for **breast** cancer, we established **breast** cancer cells stably expressing Na⁺/I⁻ symporter (**NIS**) gene that can be modulated and studied in vitro and in vivo. METHODS: We transfected rat **NIS** genes into a human **breast** cancer cell line (MCF7) by electroporation. Iodide accumulation was evaluated under various extracellular concentrations of sodium and iodide, and iodide efflux was also assessed. Biodistribution and tumor imaging were studied using tumor-bearing mice. RESULTS: A novel cell line (MCF3B), stably expressing the **NIS** gene, was established from MCF7. MCF3B took up 44 times more radioiodide in vitro than MCF7 did. Iodide uptake was completely inhibited by 1 mmol/L perchlorate and was dependent on external sodium and iodide concentrations. Iodide efflux from MCF3B cells was slower (half-life [T 1/2] > 27 min) than from FRTL5 thyroid cells (T 1/2 = 4 min). In the biodistribution study using MCF3B-xenografted mice, high tumor uptake of ¹²⁵I was shown (16.73%) at 1 h after injection, and

tumor-to-normal tissue ratios were also high (4.84-21.28), except in the stomach (0.47). However, the iodide accumulation in the tumor lessened with time, reaching less than 1% at 24 h after injection. CONCLUSION: Our preliminary data indicate that **NIS**-based gene therapy may be applied by concentrating a lethal dose of radiation in tumor cells in vivo, but further investigation is necessary to determine a method of maintaining radioiodine in the cells to allow greater therapeutic effects.

L5 ANSWER 7 OF 27 MEDLINE on STN DUPLICATE 5
 ACCESSION NUMBER: 2000182989 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10720070
 TITLE: Tissue iodine content and serum-mediated 125I uptake-blocking activity in **breast** cancer.
 AUTHOR: Kilbane M T; Ajjan R A; Weetman A P; Dwyer R; McDermott E W; O'Higgins N J; Smyth P P
 CORPORATE SOURCE: University College Dublin, St. Vincent's University Hospital, Ireland.
 SOURCE: Journal of clinical endocrinology and metabolism, (2000 Mar) 85 (3) 1245-50.
 Journal code: 0375362. ISSN: 0021-972X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: (CLINICAL TRIAL)
 Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 200003
 ENTRY DATE: Entered STN: 20000407
 Last Updated on STN: 20000407
 Entered Medline: 20000330

AB In the thyroid, active transport of iodide is under control of the TSH-dependent Na⁺/I⁻ symporter (**NIS**), whereas in the **breast** such control is less well understood. In this study, **NIS** expression was demonstrated by RT-PCR in 2 of 2 fibroadenomata and 6 of 7 **breast** carcinoma messenger ribonucleic acid isolates. In addition, mean total tissue iodine levels of 80.9 +/- 9.5 ng I/mg protein, in 23 benign tumors (fibroadenomata) were significantly higher than those in 19 **breast** cancers taken from either the tumor (18.2 +/- 4.6 ng I/mg) or morphologically normal tissue taken from within the tumor-bearing **breast** (31.8 +/- 4.9 ng I/mg; P < 0.05 in each case). Inhibition of 125I uptake into **NIS**-transfected CHO cells was observed in serum from 20 of 105 (19.0%) **breast** carcinoma, 8 of 49 (16.3%) benign **breast** disease, and 27 of 86 (31.4%) Graves' patients, but in only 1 of 33 (3.0%) age-matched female controls. IgG purified from serum of patients showing positive 125I uptake inhibition also inhibited iodide uptake, suggesting that such inhibition was antibody mediated. 125I uptake inhibition was significantly associated with thyroid peroxidase antibody positivity (P < 0.05) in sera from **breast** cancer patients, but not in those with benign **breast** disease, once again suggesting an association between thyroid autoimmunity and **breast** carcinoma.

L5 ANSWER 8 OF 27 MEDLINE on STN DUPLICATE 6
 ACCESSION NUMBER: 2000398608 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10893432
 TITLE: Molecular analysis of the sodium/iodide symporter: impact on thyroid and extrathyroid pathophysiology.
 AUTHOR: De La Vieja A; Dohan O; Levy O; Carrasco N
 CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, New York 10461, USA.
 CONTRACT NUMBER: DK-41544 (NIDDK)
 SOURCE: Physiological reviews, (2000 Jul) 80 (3) 1083-105. Ref: 132
 Journal code: 0231714. ISSN: 0031-9333.

PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824
Entered Medline: 20000816

AB The Na(+)/I(-) symporter (**NIS**) is an intrinsic membrane protein that mediates the active transport of iodide into the thyroid and other tissues, such as salivary glands, gastric mucosa, and lactating **mammary** gland. **NIS** plays key roles in thyroid pathophysiology as the route by which iodide reaches the gland for thyroid hormone biosynthesis and as a means for diagnostic scintigraphic imaging and for radioiodide therapy in hyperthyroidism and thyroid cancer. The molecular characterization of **NIS** started with the 1996 isolation of a cDNA encoding rat **NIS** and has since continued at a rapid pace. Anti-**NIS** antibodies have been prepared and used to study **NIS** topology and its secondary structure. The biogenesis and posttranslational modifications of **NIS** have been examined, a thorough electrophysiological analysis of **NIS** has been conducted, the cDNA encoding human **NIS** (hNIS) has been isolated, the genomic organization of hNIS has been elucidated, the regulation of **NIS** by thyrotropin and I(-) has been analyzed, the regulation of **NIS** transcription has been studied, spontaneous **NIS** mutations have been identified as causes of congenital iodide transport defect resulting in hypothyroidism, the roles of **NIS** in thyroid cancer and thyroid autoimmune disease have been examined, and the expression and regulation of **NIS** in extrathyroidal tissues have been investigated. In gene therapy experiments, the rat **NIS** gene has been transduced into various types of human cells, which then exhibited active iodide transport and became susceptible to destruction with radioiodide. The continued molecular analysis of **NIS** clearly holds the potential of an even greater impact on a wide spectrum of fields, ranging from structure/function of transport proteins to the diagnosis and treatment of cancer, both in the thyroid and beyond.

L5 ANSWER 9 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000:552554 CAPLUS

DOCUMENT NUMBER: 133:250509

TITLE: The **mammary** gland iodide transporter is expressed during lactation and in **breast** cancer

AUTHOR(S): Tazebay, Uygur H.; Wapnir, Irene L.; Levy, Orlie; Dohan, Orsolya; Zuckier, Lionel S.; Zhao, Qing Hua; Deng, Hou Fu; Amenta, Peter S.; Fineberg, Susan; Pestell, Richard G.; Carrasco, Nancy

CORPORATE SOURCE: Department of Molecular Pharmacology, Albert Einstein College of Medicine, Bronx, NY, 10461, USA

SOURCE: Nature Medicine (New York) (2000), 6(8), 871-878

CODEN: NAMEFI; ISSN: 1078-8956

PUBLISHER: Nature America Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The sodium/iodide symporter mediates active iodide transport in both healthy and cancerous thyroid tissue. By exploiting this activity, radioiodide has been used for decades with considerable success in the detection and treatment of thyroid cancer. Here we show that a specialized form of the sodium/iodide symporter in the **mammary** gland mediates active iodide transport in healthy lactating (but not in

nonlactating) **mammary** gland and in **mammary** tumors. In addition to characterizing the hormonal regulation of the **mammary** gland sodium/iodide symporter, we demonstrate by scintigraphy that **mammary** adenocarcinomas in transgenic mice bearing Ras or Neu oncogenes actively accumulate iodide by this symporter in vivo. Moreover, more than 80% of the human **breast** cancer samples we analyzed by immunohistochem. expressed the symporter, compared with none of the normal (nonlactating) samples from reductive mammoplasties. These results indicate that the **mammary** gland sodium/iodide symporter may be an essential **breast** cancer marker and that radioiodide should be studied as a possible option in the diagnosis and treatment of **breast** cancer.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 10 OF 27 MEDLINE on STN DUPLICATE 7
 ACCESSION NUMBER: 2001013164 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 11001757
 TITLE: Effect of prolactin on sodium iodide symporter expression in mouse **mammary** gland explants.
 AUTHOR: Rillema J A; Yu T X; Jhiang S M
 CORPORATE SOURCE: Department of Physiology, Wayne State University School of Medicine, Detroit, Michigan 48201, USA..
 jrillema@med.wayne.edu
 SOURCE: American journal of physiology. Endocrinology and metabolism, (2000 Oct) 279 (4) E769-72.
 Journal code: 100901226. ISSN: 0193-1849.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200010
 ENTRY DATE: Entered STN: 20010322
 Last Updated on STN: 20010322
 Entered Medline: 20001030

AB Iodide accumulates in milk at a concentration that is more than an order of magnitude higher than the iodide concentration in maternal plasma. In earlier studies from our laboratory, we have shown that prolactin (PRL) enhances iodide accumulation by two- to threefold in cultured **mammary** tissues taken from pregnant mice. In the present studies, we demonstrate via Western blotting techniques that prolactin elevates the quantity of the sodium iodide symporter (**NIS**) in cultured mouse **mammary** tissues. In time-course studies, the onset of the PRL effect of **NIS** accumulation was found to be between 4 and 16 h after addition of PRL to the explants. The lowest PRL concentration that elicited a significant response was 1 ng/ml, and a maximum effect was elicited with PRL concentrations >100 ng/ml. Actinomycin D, cycloheximide, and thiocyanate abolished the PRL effect on **NIS** accumulation, whereas perchlorate was without effect. These studies suggest that the PRL stimulation of iodide accumulation in milk is mediated, at least in part, by the PRL stimulation of **NIS** accumulation in **mammary** gland tissues. These studies further demonstrate that the PRL effect on **NIS** accumulation occurs via an RNA protein synthesis-dependent mechanism.

L5 ANSWER 11 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 ACCESSION NUMBER: 2000:199572 BIOSIS
 DOCUMENT NUMBER: PREV200000199572
 TITLE: The sodium iodide symporter (**NIS**), iodine and **breast** cancer.
 AUTHOR(S): Dwyer, R. M. [Reprint author]; Kilbane, M. T.; Ajjan, R. A.; Smith, D. F.; Weetman, A. P.; McDermott, E. W. M.; O'Higgins, N. J.; Smyth, P. P. A.

CORPORATE SOURCE: University College Dublin, Dublin, Ireland
SOURCE: Journal of Endocrinology, (March, 2000) Vol. 164, No. Suppl., pp. P400. print.
Meeting Info.: 19th Joint Meeting of the British Endocrine Societies, with the European Federation of Endocrine Societies. Birmingham, England, UK. March 13-16, 2000.
CODEN: JOENAK. ISSN: 0022-0795.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 17 May 2000
Last Updated on STN: 4 Jan 2002

L5 ANSWER 12 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2001:207392 BIOSIS
DOCUMENT NUMBER: PREV200100207392
TITLE: Expressions of hNIS mRNA in **breast** cancer tissues and infections of hNIS adenovirus to MCF7 **breast** cancer cells.
AUTHOR(S): Lee, S. J. [Reprint author]; Park, K.-K.; Park, K. Y.; Moon, D. H. [Reprint author]; Chang, H. [Reprint author]; Ahn, I.-M. [Reprint author]
CORPORATE SOURCE: Asan Medical Center, University of Ulsan College of Medicine, 388-1 Poongnap-dong, Songpa-gu, Seoul, 138-040, South Korea
SOURCE: Endocrine Journal, (August, 2000) Vol. 47, No. Suppl. August, pp. 240. print.
Meeting Info.: 12th International Thyroid Congress. Kyoto,, Japan. October 22-27, 2000. British Society of Gastroenterology.
ISSN: 0918-8959.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Apr 2001
Last Updated on STN: 18 Feb 2002

L5 ANSWER 13 OF 27 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2000:765817 SCISEARCH
THE GENUINE ARTICLE: 360ZA
TITLE: 'Invading edge vs. inner' (edvin) patterns of vascularization: an interplay between angiogenic and vascular survival factors defines the clinical behaviour of non-small cell lung cancer
AUTHOR: Giatromanolaki A; Koukourakis M I (Reprint); Sivridis E; OByrne K; Gatter K C; Harris A L
CORPORATE SOURCE: TUMOUR & ANGIOGENESIS RES GRP, 18 DIMOKRATIAS AVE, IRAKLION 71306, CRETE, GREECE (Reprint); DEMOCRITUS UNIV THRACE, DEPT PATHOL, ALEXANDROUPOLIS 68100, GREECE; UNIV THESSALIA, SCH MED, DEPT RADIOTHERAPY & ONCOL, LARISA 41222, GREECE; LEICESTER ROYAL INFIRM, DEPT ONCOL, LEICESTER LE1 5WW, LEICS, ENGLAND; OXFORD RADCLIFFE HOSP, DEPT CELLULAR SCI, OXFORD OX3 7LJ, ENGLAND; OXFORD RADCLIFFE HOSP, IMPERIAL CANC RES FUND, MED ONCOL UNIT, OXFORD OX3 7LJ, ENGLAND
COUNTRY OF AUTHOR: GREECE; ENGLAND
SOURCE: JOURNAL OF PATHOLOGY, (OCT 2000) Vol. 192, No. 2, pp. 140-149.
Publisher: JOHN WILEY & SONS LTD, BAFFINS LANE CHICHESTER, W SUSSEX PO19 1UD, ENGLAND.
ISSN: 0022-3417.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE; CLIN

LANGUAGE: English

REFERENCE COUNT: 38

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Neo-angiogenesis during neoplastic growth involves endothelial mitogenic and migration stimuli produced by cancer or tumour stromal cells. Although this active angiogenesis takes place in the tumour periphery, the process of vessel growth and survival in inner areas and its clinical role remain largely unexplored. The present study compared the microvessel score (MS) as well as the single endothelial cell score (ECS) in the invading edge and in inner areas of non-small cell lung carcinomas (NSCLCs). Three different patterns of vascular growth were distinguished: the edvin (edge vs. inner) type 1, where a low **NIS** was observed in both peripheral and inner tumour areas; the edvin type 2, where a high MS was noted in the invading front but a low MS in inner areas; and the edvin type 3, where both peripheral and inner tumour areas had a high MS. The ECS was high in the invading edge in edvin type 2 and 3 cases and was sharply decreased in both types in inner areas, suggesting that endothelial cell migration is unlikely to contribute to the angiogenic process in areas away from the tumour front. Expression of the vascular endothelial growth factor (VEGF) and of thymidine phosphorylase (TP) was associated with a high MS in the invading edge. VEGF was associated with a high MS in inner areas (edvin 3), while TP expression was associated with edvin type 2, showing that VEGF (and not TP) contributes to the preservation of the inner vasculature. Both edvin type 2 and 3 cases showed an increased incidence of node metastasis, but edvin type 3 cases had a poorer prognosis, even in the N1-stage group. The present study suggests that tumour factors regulating angiogenesis and vascular survival are not identical. A possible method is reported to quantify these two parameters by comparing the MS in the invading edge and inner areas (edvin types). This observation may contribute to the evaluation of the effectiveness of different therapeutic approaches, namely vascular targeting vs. antiangiogenesis, Copyright (C) 2000 John Wiley & Sons, Ltd.

L5 ANSWER 14 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:207381 BIOSIS

DOCUMENT NUMBER: PREV200100207381

TITLE: Sodium iodide transporter (**NIS**) expression in thyroid, gastroesophageal and **breast** tumors.

AUTHOR(S): Dohan, O. [Reprint author]; Paroder, M. [Reprint author]; Altorjay, A.; Fineberg, S.; Wapnir, I.; Carrasco, N. [Reprint author]

CORPORATE SOURCE: Department of Pharmacology, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY, 10461, USA

SOURCE: Endocrine Journal, (August, 2000) Vol. 47, No. Suppl. August, pp. 110. print.
Meeting Info.: 12th International Thyroid Congress. Kyoto,, Japan. October 22-27, 2000. British Society of Gastroenterology.
ISSN: 0918-8959.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 25 Apr 2001

Last Updated on STN: 18 Feb 2002

L5 ANSWER 15 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2001:199378 BIOSIS

DOCUMENT NUMBER: PREV200100199378

TITLE: Molecular analysis and pathophysiological relevance of the sodium/iodide symporter (**NIS**).

AUTHOR(S): De la Vieja, A. [Reprint author]; Dohan, O. [Reprint author]; Ginter, C. [Reprint author]; Riedel, C. [Reprint

author]; Tazebay, U. [Reprint author]; Wapnir, I.;
 Carrasco, N. [Reprint author]
 CORPORATE SOURCE: Dept. of Molecular Pharmacology, Albert Einstein College of
 Medicine, Bronx, NY, 10461, USA
 SOURCE: Endocrine Journal, (August, 2000) Vol. 47, No. Suppl.
 August, pp. 81. print.
 Meeting Info.: 12th International Thyroid Congress. Kyoto,,
 Japan. October 22-27, 2000. British Society of
 Gastroenterology.
 ISSN: 0918-8959.
 DOCUMENT TYPE: Conference; (Meeting)
 Conference; Abstract; (Meeting Abstract)
 LANGUAGE: English
 ENTRY DATE: Entered STN: 25 Apr 2001
 Last Updated on STN: 18 Feb 2002

L5 ANSWER 16 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
 ACCESSION NUMBER: 1999:143843 BIOSIS
 DOCUMENT NUMBER: PREV199900143843
 TITLE: p73 at chromosome 1p36.3 is lost in advanced stage
 neuroblastoma but its mutation is infrequent.
 AUTHOR(S): Ichimiya, Shingo; Nimura, Yoshinori; Kageyama, Hajime;
 Takada, Naoyuki; Sunahara, Masao; Shishikura, Tomotane;
 Nakamura, Yohko; Sakiyama, Shigeru; Seki, Naohiko; Ohira,
 Miki; Kaneko, Yasuhiko; McKeon, Frank; Caput, Daniel;
 Nakagawara, Akira [Reprint author]
 CORPORATE SOURCE: Div. Biochem., Chiba Cancer Cent. Res. Inst., 666-2 Nitona,
 Chiba 260-8717, Japan
 SOURCE: Oncogene, (Jan., 1999) Vol. 18, No. 4, pp. 1061-1066.
 print.
 CODEN: ONCNES. ISSN: 0950-9232.
 DOCUMENT TYPE: Article
 LANGUAGE: English
 ENTRY DATE: Entered STN: 31 Mar 1999
 Last Updated on STN: 31 Mar 1999

AB p73, a novel p53 family member, is a recently identified candidate
 neuroblastoma (NBL) suppressor gene mapped at chromosome 1p36.33 and was
 found to inhibit growth and induce apoptosis in cell lines. To test the
 hypothesis that p73 is a NBL suppressor gene. we analysed the p73 gene in
 primary human NBLs. Loss of heterozygosity (LOH) for p73 was observed in
 19% (28/151) of informative cases which included 92 mass-screening (
NIS) tumors. The hi-h frequency of p73 LOH was significantly
 associated with sporadic NBLs (9% vs 34%, $P < 0.001$), N-myc amplification
 (10% vs 71%, $P < 0.001$), and advanced stage (14% vs 28%, $P < 0.05$). Both
 p73alpha and p73beta transcripts were detectable in only 46 of 134 (34%)
 NBLs at low levels by RT-PCR methods, while they were easily detectable in
 most **breast** cancers and colorectal cancers under the same
 conditions. They found no correlation between p73 LOH and its expression
 levels ($P > 0.1$). We found two mutations out of 140 NBLs, one somatic and
 one germline, which result in amino acid substitutions in the C-terminal
 region of p73 which may affect transactivation functions. though, in the
 same tumor samples. no mutation of the p53 gene was observed as reported
 previously. These results suggest that allelic loss of the p73 gene may
 be a later event in NBL tumorigenesis. However, p73 is infrequently
 mutated in primary NBLs and may hardly function as a tumor suppressor in a
 classic Knudson's manner.

L5 ANSWER 17 OF 27 MEDLINE on STN DUPLICATE 8
 ACCESSION NUMBER: 2000044587 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 10576759
 TITLE: Sodium/iodide symporter: a key transport system in thyroid
 cancer cell metabolism.
 AUTHOR: Filetti S; Bidart J M; Arturi F; Caillou B; Russo D;

Schlumberger M
CORPORATE SOURCE: Dipartimento di Medicina Sperimentale e Clinica, Universita
di Catanzaro, 88100 Catanzaro, Italy.. filetti@tin.it
SOURCE: European journal of endocrinology / European Federation of
Endocrine Societies, (1999 Nov) 141 (5) 443-57.
Ref: 69
Journal code: 9423848. ISSN: 0804-4643.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199912
ENTRY DATE: Entered STN: 20000113
Last Updated on STN: 20000113
Entered Medline: 19991228

AB The recent cloning of the gene encoding the sodium/iodide symporter (**NIS**) has enabled better characterization of the molecular mechanisms underlying iodide transport, thus opening the way to clarifying its role in thyroid diseases. Several studies, at both the mRNA and the protein expression levels, have demonstrated that TSH, the primary regulator of iodide uptake, upregulates **NIS** gene expression and **NIS** protein abundance, both in vitro and in vivo. However, other factors, including iodide, retinoic acid, transforming growth factor-beta, interleukin-lalpha and tumour necrosis factor alpha, may participate in the regulation of **NIS** expression. Investigation of **NIS** mRNA expression in different thyroid tissues has revealed increased levels of expression in Graves' disease and toxic adenomas, whereas a reduction or loss of **NIS** transcript was detected in differentiated thyroid carcinomas, despite the expression of other specific thyroid markers. **NIS** mRNA was also detected in non-thyroid tissues able to concentrate radioiodine, including salivary glands, stomach, thymus and **breast**. The production of specific antibodies against the **NIS** has facilitated study of the expression of the symporter protein. Despite of the presence of high levels of human (h)**NIS** mRNA, normal thyroid glands exhibit a heterogeneous expression of **NIS** protein, limited to the basolateral membrane of the thyrocytes. By immunohistochemistry, staining of h**NIS** protein was stronger in Graves' and toxic adenomas and reduced in thyroid carcinomas. Measurement of iodide uptake by thyroid cancer cells is the cornerstone of the follow-up and treatment of patients with thyroid cancer. However, radioiodide uptake is found only in about 67% of patients with persistent or recurrent disease. Several studies have demonstrated a decrease in or a loss of **NIS** expression in primary human thyroid carcinomas, and immunohistochemical studies have confirmed this considerably decreased expression of the **NIS** protein in thyroid cancer tissues, suggesting that the low expression of **NIS** may represent an early abnormality in the pathway of thyroid cell transformation, rather than being a consequence of cancer progression. The relationship between radioiodine uptake and **NIS** expression by thyroid cancer cells require further study. New strategies, based on manipulation of **NIS** expression, to obtain **NIS** gene reactivation or for use as **NIS** gene therapy in the treatment of radiosensitive cancer, are also being investigated.

L5 ANSWER 18 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 1999:541081 BIOSIS
DOCUMENT NUMBER: PREV199900541081
TITLE: Defective iodination within the **breast**: A feature
of **breast** carcinoma?.
AUTHOR(S): Dwyer, R. [Reprint author]; Kilbane, M. T. [Reprint
author]; Smyth, P.P.A.; Ajjan, R. A.; Weetman, A. P.;

McDermott, E.W.M. [Reprint author]; O'Higgins, N. J.
[Reprint author]
CORPORATE SOURCE: Surgery, UCD, Dublin, Ireland
SOURCE: European Journal of Cancer, (Sept., 1999) Vol. 35, No.
SUPPL. 4, pp. S199. print.
Meeting Info.: ECCO 10: The European Cancer Conference.
Vienna, Austria. September 12-16, 1999. Federation of
European Cancer Societies.
CODEN: EJCAEL. ISSN: 0959-8049.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Dec 1999
Last Updated on STN: 10 Dec 1999

L5 ANSWER 19 OF 27 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1998251597 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9589686
TITLE: Analysis of human sodium iodide symporter gene expression
in extrathyroidal tissues and cloning of its complementary
deoxyribonucleic acids from salivary gland, **mammary**
gland, and gastric mucosa.
COMMENT: Comment in: J Clin Endocrinol Metabolism 1999 Feb;84(2):821-2.
PubMed ID: 10022463
AUTHOR: Spitzweg C; Joba W; Eisenmenger W; Heufelder A E
CORPORATE SOURCE: Molecular Thyroid Research Unit Medizinische Klinik,
Klinikum Innenstadt, Ludwig-Maximilians-Universitat,
Munchen, Germany.
SOURCE: Journal of clinical endocrinology and metabolism,
(1998 May) 83 (5) 1746-51.
Journal code: 0375362. ISSN: 0021-972X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980611
Last Updated on STN: 20000303
Entered Medline: 19980604

AB The ability to concentrate iodide is a fundamental property of normally functioning thyroid tissue and represents the first step in the production of thyroid hormones. Iodide uptake has been demonstrated in various extrathyroidal tissues, including salivary gland, gastric mucosa, and lactating **mammary** gland. Recently, cloning and molecular characterization of the human sodium iodide symporter (hNIS) have been reported; however, the patterns of hNIS gene expression in human tissues have remained unidentified. To examine the profiles of human hNIS gene expression in various normal human tissues, we performed high-stringency Northern blot analysis using a 32P-labeled hNIS-specific complementary DNA (cDNA) probe (nucleotides 1184-1667). To detect rare hNIS transcripts in small tissue samples, RT-PCR was performed with a pair of hNIS-specific oligonucleotide primers designed to amplify a portion (nucleotides 1184-1667) of the hNIS gene. hNIS-specific transcripts were confirmed by Southern hybridization using a digoxigenin-labeled internal hNIS-specific oligonucleotide probe (nucleotides 1460-1477). To monitor cDNA integrity and quantity, and to rule out DNA contamination and illegitimate transcription, all samples were coamplified with two pairs of intron-spanning primers designed to amplify fragments of the human beta-actin and thyroglobulin genes, respectively. Using Northern blot analysis, hNIS transcripts of approximately 4 kb were detected in thyroid gland and parotid gland but not in a broad range of endocrine and nonendocrine tissues. RT-PCR and Southern hybridization revealed hNIS

gene expression in thyroid gland, salivary gland, parotid gland, submandibular gland, pituitary gland, pancreas, testis, **mammary** gland, gastric mucosa, prostate and ovary, adrenal gland, heart, thymus, and lung. By contrast, hNIS transcripts were not detected in normal orbital fibroblasts, colon, and nasopharyngeal mucosa. To further analyze hNIS gene sequences in parotid gland, **mammary** gland, and gastric mucosa, the EXPAND High Fidelity PCR System and three sets of overlapping **NIS** oligonucleotide primers were used for amplification and cloning. The resulting PCR products were subcloned into pBluescript-SKII(-)vector, and at least two independent cDNA clones derived from each tissue were subjected to automated sequencing. The nucleotide sequences of hNIS cDNA derived from parotid gland, **mammary** gland, and gastric mucosa revealed full identity with the recently published human thyroid-derived **NIS** cDNA sequence. In conclusion, our results demonstrate markedly variable levels of hNIS gene expression in several extrathyroidal tissues. Although the physiological role of hNIS in these tissues awaits further study, our results suggest that the capacity to actively transport iodine may be a feature common to several secretory and endocrine tissues. The diminished capacity to transport and concentrate iodide in extrathyroidal tissues (such as parotid gland, **mammary** gland, and gastric mucosa), compared with thyroid gland, does not seem to be caused by an altered primary structure of the hNIS cDNA. Variability of **NIS** gene expression levels in normal extrathyroidal tissues may rather be caused by differences in **NIS** gene transcriptional activity. Further studies will address this hypothesis and examine the mechanisms of tissue-specific regulation of **NIS** gene expression.

L5 ANSWER 20 OF 27 MEDLINE on STN DUPLICATE 10
 ACCESSION NUMBER: 1999093631 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9876351
 TITLE: Regulation and tissue distribution of the human sodium iodide symporter gene.
 AUTHOR: Ajjan R A; Kamaruddin N A; Crisp M; Watson P F; Ludgate M; Weetman A P
 CORPORATE SOURCE: Department of Medicine, University of Sheffield, UK.
 SOURCE: Clinical endocrinology, (1998 Oct) 49 (4) 517-23.
 Journal code: 0346653. ISSN: 0300-0664.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199901
 ENTRY DATE: Entered STN: 19990128
 Last Updated on STN: 19990128
 Entered Medline: 19990111

AB OBJECTIVE: Iodide uptake by the thyroid gland is mediated by the sodium iodide symporter (**NIS**). In the present report, we have analysed the factors that modulate human **NIS** mRNA expression and iodide uptake in primary thyroid follicular cell (TFC) cultures. In addition, **NIS** mRNA tissue distribution was investigated. METHODS: Primary thyroid follicular cell cultures were treated with human recombinant TSH with or without cytokines for 72 h. Subsequently, **NIS** gene expression and iodide uptake were analysed using reverse transcription-polymerase chain reaction (RT-PCR) and ¹²⁵I uptake, respectively. Human tissue samples were investigated for **NIS** gene expression using both RT-PCR and Northern blotting. RESULTS: Human TSH increased both **NIS** gene expression and iodide uptake in TFC cultures in a dose-dependent manner. Using concentrations of 0.1 U/l of hTSH, a minor increase in **NIS** gene expression was detected without a detectable increase in iodide uptake. IL-1 alpha, TNF alpha and IFN gamma at concentrations of 10(5) U/l all inhibited TSH-induced **NIS** gene expression and iodide uptake. In these experiments,

there was a good correlation between **NIS** mRNA expression and iodide uptake. Using RT-PCR higher levels of **NIS** mRNA were detected in Graves' disease (GD) compared to multi-nodular goitre tissue samples. Stomach and salivary gland tissue also expressed **NIS** mRNA, whereas low levels were found in the **mammary** gland and extraocular muscle tissue. No expression was detected in the ovary, oesophagus, colon, extraocular fat or skin. In contrast, Northern blot analysis failed to detect **NIS** in stomach, salivary gland, intestinal fat or non-toxic multi-nodular goitre tissue samples, although this was present in GD thyroid tissue. CONCLUSION: TSH upregulates sodium iodide symporter gene expression and iodide uptake in primary thyroid follicular cell cultures, and this induction is modulated by cytokines. Variable levels of sodium iodide symporter mRNA are present in different tissue samples, with high expression evident in Graves' disease thyroid tissue.

L5 ANSWER 21 OF 27 MEDLINE on STN DUPLICATE 11
 ACCESSION NUMBER: 1999062594 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9846164
 TITLE: The sodium iodide symporter gene and its regulation by cytokines found in autoimmunity.
 AUTHOR: Ajjan R A; Watson P F; Findlay C; Metcalfe R A; Crisp M; Ludgate M; Weetman A P
 CORPORATE SOURCE: Department of Medicine, University of Sheffield Clinical Sciences Centre, Northern General Hospital, Sheffield, UK.
 SOURCE: Journal of endocrinology, (1998 Sep) 158 (3) 351-8.
 Journal code: 0375363. ISSN: 0022-0795.
 PUB. COUNTRY: ENGLAND: United Kingdom
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199812
 ENTRY DATE: Entered STN: 19990115
 Last Updated on STN: 19990115
 Entered Medline: 19981216

AB Iodide concentration by the thyroid gland, an essential step for thyroid hormone synthesis, is mediated by the Na⁺/I⁻ symporter (**NIS**). To identify factors that may regulate this process, we have studied **NIS** gene expression in the Fisher rat thyroid cell line (FRTL-5) by a semi-quantitative reverse transcription-polymerase chain reaction (RT-PCR) technique. Increasing concentrations of bovine TSH (0.1, 1, 10, 50 and 100 mU/l), with or without tumour necrosis factor-alpha (TNF alpha), interferon-gamma (IFN gamma) or interleukin-1 alpha (IL-1 alpha) were added to FRTL-5 cells previously deprived of TSH for a minimum of 5 days. RNA was extracted and samples were studied for **NIS** expression. TSH enhanced **NIS** mRNA expression in a dose-dependent manner, with induction evident at 0.1 mU/l, reaching a peak at 50 mU/l, an effect detected after 6 h of stimulation, but not in the first 2 h. Both TNF alpha and, to a lesser extent, IL-1 alpha inhibited basal and TSH-induced **NIS** expression. High concentrations of IFN gamma also downregulated TSH-stimulated **NIS** mRNA expression. Using the same technique, we also investigated **NIS** mRNA tissue distribution in two male and one female Wistar rats. High levels of **NIS** expression were detected in the thyroid, stomach, and **mammary** gland, lower levels were found in the intestine, adipose tissue and liver, borderline levels were expressed in the salivary gland, and no expression was detected in the kidneys. In summary, we have shown that TSH upregulates rat **NIS** gene expression in vitro, and this induction can be modulated by cytokines. Analysis of the distribution of rat **NIS** mRNA ex vivo demonstrated variable levels of **NIS** transcription in different tissue samples.

L5 ANSWER 22 OF 27 CAPLUS COPYRIGHT 2004 ACS on STN
 ACCESSION NUMBER: 1999:9314 CAPLUS
 DOCUMENT NUMBER: 130:220763
 TITLE: Characterization of gastric Na⁺/I⁻ symporter of the rat
 AUTHOR(S): Kotani, Tomio; Ogata, Yoshikazu; Yamamoto, Ikuo; Aratake, Yatsuki; Kawano, Jun-Ichi; Suganuma, Tatsuo; Ohtaki, Sachiya
 CORPORATE SOURCE: Department of Laboratory Medicine, Miyazaki Medical College Hospital, Miyazaki, 889-1692, Japan
 SOURCE: Clinical Immunology and Immunopathology (1998), 89(3), 271-278
 CODEN: CLIIAT; ISSN: 0090-1229
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB Characterization of gastric Na⁺/I⁻ symporter (**NIS**) of the rat was carried out. Sequencing of the open reading frame of gastric **NIS** mRNA showed only three nucleotide changes when compared with FRTL-5 **NIS** cDNA, and two of these changes led to amino acid changes. The results of Northern blot anal. showed that abundant **NIS** mRNA was expressed in the stomach when compared with other organs. Western blot anal. using gastric mucosa and FRTL-5 lysates detected the difference in mol. weight between FRTL-5 and gastric mucosa lysates, suggesting abnormal posttranslational modification of gastric **NIS** protein. Immunohistochem., gastric **NIS** protein was located in the cornification layer of the stratified squamous epithelium of the pars proventricularis and in parietal cells and on the apical border of surface epithelial cells of the pars glandularis. Gastric **NIS** protein was present in tubulovesicular structures and lysosomes in parietal cells by immunoelectron microscopy. Gastric **NIS** protein exists to trap I⁻ from the gastric lumen, except in parietal cells. Results indicated that a very large amount of gastric **NIS** mRNA is expressed to be translated, whereas only a small amount of immature gastric **NIS** protein is detected. This may indicate that immature gastric **NIS** protein rapidly degrades to peptides.
 (c) 1998 Academic Press.

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 23 OF 27 MEDLINE on STN DUPLICATE 12
 ACCESSION NUMBER: 1999119623 MEDLINE
 DOCUMENT NUMBER: PubMed ID: 9921055
 TITLE: [Treatment of **breast** carcinoma at the Military Hospital in **Nis** 1986-1995].
 Lecenje karcinoma dojke u Vojnoj bolnici u Nisu 1986-1995. godine.
 AUTHOR: Pecanac R; Petkovic A; Tomic V; Kovinic M
 SOURCE: Vojnosanitetski pregled. Military-medical and pharmaceutical review, (1998 Sep-Oct) 55 (5 Suppl) 11-6.
 Journal code: 21530700R. ISSN: 0042-8450.
 PUB. COUNTRY: Yugoslavia
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: Serbian
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199902
 ENTRY DATE: Entered STN: 19990301
 Last Updated on STN: 19990301
 Entered Medline: 19990218

L5 ANSWER 24 OF 27 MEDLINE on STN DUPLICATE 13
 ACCESSION NUMBER: 97194875 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9042313
TITLE: Nucleolar volume in **breast** carcinomas.
AUTHOR: Mihailovic D; Ilic R; Dordevic B; Radic S
CORPORATE SOURCE: Institute of Pathology, University of Nis, Serbia,
Yugoslavia.
SOURCE: Anticancer research, (1996 Nov-Dec) 16 (6C)
3919-21.
Journal code: 8102988. ISSN: 0250-7005.
PUB. COUNTRY: Greece
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970313

AB The prognostic value of histopathological typing of **breast** carcinomas is relatively good. The determination of cell size has been a common and useful parameter in the diagnosis of various malignancies. With modern stereologic methods it is possible to obtain unbiased estimates of nucleolar volume. The aim of this study was to present our data regarding the nucleolar size in **breast** carcinoma. Patients treated for **breast** carcinoma (n = 39) were retrieved and randomly selected from the files of the University Institute of Pathology, **Nis**. Histological sections (4 microns) were cut from each of the routinely processed, paraffin-embedded tissue blocks and stained with hematoxylin and eosin. A Carl Zeiss NU-1 microscope equipped with a x 100 oil-immersion lens (N.A. = 1.25) and eyepiece graticule was used for stereological measurements. A total magnification of x 1600 was used. A simple grid was used for point sampling of nucleolar intercepts, which were measured in one arbitrary direction. By multiplying the averaged, cubed intercept length by $\pi/3$, an unbiased estimate of volume-weighted nucleolar volume was obtained. The nucleolar volume was significantly larger in invasive ductal carcinoma (12.34 +/- 3.48 microns³) than invasive lobular carcinoma (5.6 +/- 2.73 microns³) and mucinous (colloid) adenocarcinoma (0.88 +/- 0.42 micron³). Various histological types of **breast** cancer exhibit differences with regard to nucleolar volume.

L5 ANSWER 25 OF 27 MEDLINE on STN
ACCESSION NUMBER: 2002589016 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12222274
TITLE: Country news: focus on Moldova.
AUTHOR: Kunz K
SOURCE: Entre nous (Copenhagen, Denmark), (1996 Sep) (33)
11.
Journal code: 9515186. ISSN: 1014-8485.
Report No.: PIP-118940; POP-00260191.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Population
ENTRY MONTH: 199703
ENTRY DATE: Entered STN: 20021101
Last Updated on STN: 20021101
Entered Medline: 19970304

AB Moldova, like other newly independent states (**NIS**), is in urgent need of health education materials that address reproductive health and family planning concerns in the local language. The lack of such information has been cited as a major factor in the alarming rise in sexually transmitted disease (STD) transmission in Eastern Europe. A recent family health education mission to Moldova developed a strategy for a successful campaign. Health care professionals will be the first target group. A series of seminars and workshops will be directed at sex

education teachers, hospital personnel, mass media representatives, and other relevant groups. In addition, four weekly television programs on **breast** feeding, infertility, STDs, and reproductive health are scheduled and simple informational brochures will be distributed. The plan will be linked to Healthy Lifestyle initiatives in the state.

L5 ANSWER 26 OF 27 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 14

ACCESSION NUMBER: 1980:176972 BIOSIS
DOCUMENT NUMBER: PREV198069051968; BA69:51968
TITLE: INDUCTION OF CHROMOSOMAL ABERRATIONS IN CULTURED MAMMALIAN
CELLS BY NICKEL COMPOUNDS.
AUTHOR(S): NISHIMURA M [Reprint author]; UMEDA M
CORPORATE SOURCE: TISSUE CULT LAB, YOKOHAMA CITY UNIV SCH MED, URAFUNO,
MINAMI, YOKOHAMA, KANAGAWA 232, JPN
SOURCE: Mutation Research, (1979) Vol. 68, No. 4, pp. 337-350.
CODEN: MUREAV. ISSN: 0027-5107.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: ENGLISH

AB The effects of 4 Ni compounds, nickel chloride ($\text{NiCl}_2 \cdot 6\text{H}_2\text{O}$)
nickel acetate $(\text{CH}_3\text{COO})_2\text{Ni} \cdot 4\text{H}_2\text{O}$ potassium cyanonickelate K_2Ni
 $(\text{CN})_4 \cdot \text{H}_2\text{O}$ and nickel sulfide (**NiS**) were studied in a
line of **mammary** carcinoma cells from the C3H mouse. All 4 were
easily taken up by the cells and reacted with protein, RNA and possibly
DNA. Measurements of Leu, uridine and thymidine uptake during exposure
showed that the syntheses of protein and DNA were more sensitive than RNA.
Chromosomal aberrations were observed during the recovery period following
the end of the treatment with Ni. The implications of these results were
discussed with respect to the carcinogenicity of the compounds and to the
recommended protocols for mutagenicity testing by chromosomal aberrations.
(Human applicability is implied.).

L5 ANSWER 27 OF 27 MEDLINE on STN DUPLICATE 15

ACCESSION NUMBER: 80011436 MEDLINE
DOCUMENT NUMBER: PubMed ID: 481448
TITLE: Inducibility of chromosomal aberrations by metal compounds
in cultured mammalian cells.
AUTHOR: Umeda M; Nishimura M
SOURCE: Mutation research, (1979 Jul) 67 (3) 221-9.
Journal code: 0400763. ISSN: 0027-5107.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197911
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19791121

AB Metal compounds were tested for their ability to induce chromosomal
aberrations in cultured mammalian cells. Chromosomal aberrations were
induced by the application of some Cr, Mn and Ni compounds. Among
6-valent Cr compounds, $\text{K}_2\text{Cr}_2\text{O}_7$ and CrO_3 induced high levels of
aberrations, at rates which were similar for Cr-equivalent doses. The
perchromate compounds were more efficient in producing chromosomal
aberrations than was a chromate compound, K_2CrO_4 . A 3-valent Cr compound,
 $\text{Cr}_2(\text{SO}_4)_3$, was less toxic and failed to induce a demonstrable increase in
chromosomal aberrations. KMnO_4 induced aberrations, but at a low rate.
As to Ni compounds, NiCl_2 and $(\text{CH}_3\text{COO})_2\text{Ni}$ induced few aberrations.
Administration of $\text{K}_2\text{Ni}(\text{CN})_4$ induced only gaps. **NiS** induced a
low but definite increase in chromosomal aberrations. The rate of these
aberrations increased with an increase in treatment time from 24 to 48 h,
indicating a time-dependent increase in the hereditary toxicity of metal

compounds. CdCl₂ and HgCl₂ were somewhat toxic, but failed to induce chromosomal aberrations in the present study.

=>

=> log h

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

70.19

70.82

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

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